Linking risk factors and disease origins in breast cancer

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Researchers from the Geisel School of Medicine at Dartmouth have found that epigenetic changes to DNA are associated with aging in disease-free breast tissues and are further altered in breast tumors. Epigenetic changes describe heritable alterations caused by mechanisms other than by changes in DNA sequence. The discovery, published in the February 2014 issue of *Epigenetics*, illustrates how cancer and aging are tightly interconnected processes by identifying epigenetic alterations present in the normal aging breast that may increase disease risk in cancer-free individuals.

The epigenetic changes examined highlight different patterns in DNA methylation, which involves the chemical modification of DNA and acts in the control of gene expression. While DNA methylation is a normal and necessary epigenetic process, breast tumors exhibit altered methylation patterns compared to normal breast tissue. Accordingly, atypical DNA methylation marks are recognized to precede cancer initiation.

For the study, the researchers leveraged publicly available genome-wide methylation data on disease-free breast tissues and identified consistent methylation alterations associated with the aging process across multiple populations. The levels of methylation in normal tissues were then compared to breast tumor tissues where age-related changes were further altered in breast tumors. Their data suggests that there may be common genomic regions that are particularly susceptible to changes in DNA methylation over time in disease-free breast tissue (or that these changes

are selected for) on the path to development of cancer.

Although age is the strongest demographic risk factor for breast cancer, the mechanisms underlying how age increases a woman's risk for the development of disease are incompletely characterized. Emerging literature has demonstrated that aging can have profound effects on DNA methylation patterns that reflect an accumulation of exposures. Hence, the study extends the understanding of the biological mechanisms through which an established breast cancer risk factor, such as age, contributes to carcinogenesis.

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